Baskar, P.
10/633835

FILE 'REGISTRY' ENTERED AT 11:24:05 ON 06 MAR 2006
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STRUCTURE FILE UPDATES: 5 MAR 2006 HIGHEST RN 875875-45-9
DICTIONARY FILE UPDATES: 5 MAR 2006 HIGHEST RN 875875-45-9

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**********************************************************************
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* The CA roles and document type information have been removed from  *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
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http://www.cas.org/ONLINE/UG/regprops.html

- key terms

```
                E ACETYL COA CARBOXYLASE/CN 5
L1             17 S ACETYL COA CARBOXYLASE ?/CN
                E BIOTIN CARBOXYLASE/CN 5
L2            135 S BIOTIN CARBOXYLASE?/CN

                E SORAPHEN/CN
L5             19 S E11 OR E16-25 OR E28-36
```

FILE 'CAPLUS' ENTERED AT 11:24:05 ON 06 MAR 2006
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FILE COVERS 1907 - 6 Mar 2006 VOL 144 ISS 11
FILE LAST UPDATED: 5 Mar 2006 (20060305/ED)

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L1 17 SEA FILE=REGISTRY ABB=ON PLU=ON ACETYL COA CARBOXYLASE ?/CN
L2 135 SEA FILE=REGISTRY ABB=ON PLU=ON BIOTIN CARBOXYLASE?/CN
L5 19 SEA FILE=REGISTRY ABB=ON PLU=ON "SORAPHEN A"/CN OR ("SORAPHEN A1A"/CN OR "SORAPHEN B"/CN OR "SORAPHEN C"/CN OR "SORAPHEN D"/CN OR "SORAPHEN E"/CN OR "SORAPHEN F"/CN OR "SORAPHEN H"/CN OR "SORAPHEN J"/CN OR "SORAPHEN M"/CN OR "SORAPHEN N"/CN) OR ("SORAPHEN Q"/CN OR "SORAPHEN R"/CN OR "SORAPHEN S"/CN OR "SORAPHEN T"/CN OR "SORAPHEN U"/CN OR "SORAPHEN V"/CN OR "SORAPHEN X"/CN OR "SORAPHEN Y"/CN OR "SORAPHEN Z"/CN)
L6 8201 SEA FILE=CAPLUS ABB=ON PLU=ON L1 OR (AC OR ACETYL)(W)(COA OR (COENZYME OR CO ENZYME OR CO)(W)A)(W)CARBOXYLASE OR ACCASE OR ACC
L7 145 SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (L2 OR BIOTIN CARBOXYLASE OR BC)
L8 5 SEA FILE=CAPLUS ABB=ON PLU=ON L7 AND (L5 OR SORAPHEN)

L8 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 17 Feb 2006
ACCESSION NUMBER: 2006:149488 CAPLUS
DOCUMENT NUMBER: 144:187043
TITLE: Crystal structure of **biotin carboxylase** domain of **acetyl-coenzyme A carboxylase** and its use for molecular modeling of modulators
INVENTOR(S): Shen, Yang; Volrath, Sandra L.; Weatherly, Stephanie C.; Elich, Tedd D.; Anderson, Richard; Tong, Liang
PATENT ASSIGNEE(S): Cropsolution, Inc., USA
SOURCE: PCT Int. Appl., 483 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006017515	A2	20060216	WO 2005-US27440	20050803

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR,

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-599831P P 20040806

US 2004-637068P P 20041217

AB The crystal structure atomic coordinates are provided for a **biotin carboxylase** (**BC**) domain of yeast **acetyl-CoA carboxylase** (**ACC**) as free enzyme at 2.9 Å resolution and in complex with **soraphen** A at 1.8 Å resolution. Homol. modeling of yeast **ACC** may be employed to solve the structures of **BC** domains of other **ACC** species, including those of Magnaporthe, Ustilago maydis, Phytophthora infestans, human ACC1 and ACC2, and mouse. The invention also provides computer-based methods for identifying compds. that modulates activity of **ACC**, a computer-based method for rationally designing a compound that modulates activity of **ACC**, along with compds. produced by such methods. The structures suggest that **soraphen** may have a novel mechanism of inhibiting the **BC** domain by binding in the dimer interface, thereby disrupting the oligomerization of this domain, which is crucial for its catalytic activity. A fluorescence-based binding assay allowed characterization of the effects of single site mutations in the **soraphen** binding site on inhibitor sensitivity. Agrochem. and pharmaceutical uses of **ACC** modulators are also provided (no data).

IT **9075-71-2D, Biotin carboxylase**, complex with **soraphen** A **122547-72-2D, Soraphen** A, complex with **acetyl-CoA carboxylase**
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(crystal structure of **biotin carboxylase** domain of **acetyl-CoA carboxylase** and its use for mol. modeling of modulators)

L8 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 17 Jan 2005
ACCESSION NUMBER: 2005:38098 CAPLUS
DOCUMENT NUMBER: 142:214253
TITLE: A mechanism for the potent inhibition of eukaryotic **acetyl-coenzyme A carboxylase** by **soraphen** A, a macrocyclic polyketide natural product
AUTHOR(S): Shen, Yang; Volrath, Sandra L.; Weatherly, Stephanie C.; Elich, Tedd D.; Tong, Liang
CORPORATE SOURCE: Department of Biological Sciences, Columbia University, New York, NY, 10027, USA
SOURCE: Molecular Cell (2004), 16(6), 881-891
CODEN: MOCEFL; ISSN: 1097-2765
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Acetyl-CoA carboxylases** (**ACCs**) have crucial roles in fatty acid metabolism **Soraphen** A, a macrocyclic polyketide natural product, is a nanomolar inhibitor against the **biotin carboxylase** (**BC**) domain of human, yeast, and other eukaryotic **ACCs**. Here we

report the crystal structures of the yeast **BC** domain, alone and in complex with **soraphen** A. **Soraphen** has extensive interactions with an allosteric site, about 25 Å from the active site. The specificity of **soraphen** is explained by large structural differences between the eukaryotic and prokaryotic **BC** in its binding site, confirmed by our studies on the effects of single-site mutations in this binding site. Unexpectedly, our structures suggest that **soraphen** may bind in the **BC** dimer interface and inhibit the **BC** activity by disrupting the oligomerization of this domain. Observations from native gel electrophoresis confirm this structural insight. The structural information provides a foundation for structure-based design of new inhibitors against these enzymes.

IT **9075-71-2, Biotin carboxylase**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(crystal structures suggest **soraphen** A binding disrupts oligomerization of **biotin carboxylase** domain in yeast **acetyl-CoA carboxylase**)

IT **122547-72-2D, Soraphen** A, complexes with **BC** domain
RL: PRP (Properties)
(crystal structures suggest **soraphen** A binding disrupts oligomerization of **biotin carboxylase** domain in yeast **acetyl-CoA carboxylase**)

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 10 Jun 2004
ACCESSION NUMBER: 2004:468907 CAPLUS
DOCUMENT NUMBER: 141:152893
TITLE: Expression and characterization of recombinant fungal **acetyl-CoA carboxylase** and isolation of a **soraphen**-binding domain
AUTHOR(S): Weatherly, Stephanie C.; Volrath, Sandra L.; Elich, Tedd D.
CORPORATE SOURCE: Cropsolution, Inc., Research Triangle Park, NC, 27560, USA
SOURCE: Biochemical Journal (2004), 380(1), 105-110
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Actyl-CoA carboxylase (**ACC**) catalyzes the 1st step in fatty acid biosynthesis. Owing to its role in primary metabolism, **ACC** has been exploited as a com. herbicide target and identified as a chemical validated fungicide target. In animals, **ACC** is also a key regulator of lipid metabolism This function has made **ACC** a prime target for the development of antiobesity and anti-type II diabetes therapeutics. Despite its economic importance, there is a lack of published information on the recombinant expression of **ACC**. Here, the authors report the expression of enzymically active fungal (Ustilago maydis) **ACC** in Escherichia coli. The recombinant enzyme exhibited Km values of 0.14 and 0.19 mM for acetyl-CoA and ATP resp., which were comparable with those reported for the endogenous enzyme. The polyketide natural product,

soraphen A, is a potent inhibitor of the **biotin carboxylase** (**BC**) domain of endogenous fungal **ACC**. Similarly, recombinant **ACC** activity was inhibited by **soraphen** A with a Ki of 2.1 nM. A truncated **BC** domain that included amino acids 2-560 of the full-length protein was also expressed in E. coli. The isolated **BC** domain was expressed to higher levels, and was more stable than full-length **ACC**. Although incapable of enzymic turnover, the **BC** domain exhibited high-affinity **soraphen** A binding (Kd = 1.1 nM), demonstrating a native conformation. Addnl. **BC** domains from the phytopathogenic fungi, Magnaporthe grisea and Phytophthora infestans, were also cloned and expressed, and were shown to exhibit high-affinity **soraphen** A binding. Together, these reagents will be useful for structural studies and assay development.

IT **9075-71-2P, Biotin carboxylase**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(expression in Escherichia coli and purification and characterization of recombinant fungal **acetyl-CoA carboxylase** and purification of **soraphen** A-binding **biotin carboxylase** domain)

IT **122547-72-2, Soraphen** A
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression in Escherichia coli and purification and characterization of recombinant fungal **acetyl-CoA carboxylase** and purification of **soraphen** A-binding **biotin carboxylase** domain)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 13 Feb 2004
ACCESSION NUMBER: 2004:120870 CAPLUS
DOCUMENT NUMBER: 140:176293
TITLE: Sequences of fungal and human **acetyl CoA carboxylase** and recombinant **biotin carboxylase** domains for identification of **acetyl CoA carboxylase** inhibitors
INVENTOR(S): Elich, Tedd D.; Volrath, Sandra L.; Weatherly, Stephanie C.
PATENT ASSIGNEE(S): Cropsolution, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013159	A2	20040212	WO 2003-US24356	20030804
WO 2004013159	A3	20050909		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,

LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

CA 2494268	AA	20040212	CA 2003-2494268	20030804
US 2004086994	A1	20040506	US 2003-633835	20030804
EP 1572722	A2	20050914	EP 2003-767154	20030804
EP 1572722	A3	20051102		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2006500013	T2	20060105	JP 2004-526405	20030804
PRIORITY APPLN. INFO.:			US 2002-401170P P	20020805
			WO 2003-US24356 W	20030804

AB A peptide comprising an **Acetyl CoA carboxylase** (**ACCase**) having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional **biotin carboxylase** (**BC**) domain is described. **ACCase** is selected from the group consisting of mammal, insect, yeast, Ascomycota, Basidiomycota, and Oomycota **ACCase**. The protein sequence of the peptide described above and a recombinant host cell that contains the nucleic acid and expresses the encoded peptide is also described. A method of identifying **Acetyl CoA carboxylase** inhibitors, fungicides, is also described herein.

IT **128481-23-2, Soraphens**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(binding to **acetyl CoA carboxylase**; sequences of fungal and human **acetyl CoA carboxylase** and recombinant **biotin carboxylase** domains for identification of **acetyl CoA carboxylase** inhibitors)

L8 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 19 Jul 1995
ACCESSION NUMBER: 1995:682905 CAPLUS
DOCUMENT NUMBER: 123:78448
TITLE: Selection, cloning of gene for, and purification of yeast **acetyl-CoA carboxylase** resistant to **soraphen** A.
INVENTOR(S): Vahlensieck, Hans-Friedrich; Hinnen, Albert
PATENT ASSIGNEE(S): Ciba-Geigy AG, Switz.; Syngenta Participations AG
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 658622	A2	19950621	EP 1994-810710	19941208
EP 658622	A3	19990630		
EP 658622	B1	20030521		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 241009	E	20030615	AT 1994-810710	19941208
PT 658622	T	20031031	PT 1994-810710	19941208
ES 2199223	T3	20040216	ES 1994-810710	19941208
US 5641666	A	19970624	US 1994-354973	19941213
JP 07203966	A2	19950808	JP 1994-333986	19941216
US 6153374	A	20001128	US 1995-469708	19950606
PRIORITY APPLN. INFO.:			GB 1993-25819 A	19931217
			US 1994-354973 A3	19941213

AB The present invention discloses DNA mols. comprising a gene encoding yeast **acetyl-CoA carboxylase** resistant to **soraphen** A inhibition. Mutations conferring **soraphen** A resistance to **acetyl-CoA carboxylase** can be dominant or recessive, and they can be point mutations, deletion or insertion mutations. In addition methods of isolating a gene encoding fungal **acetyl-CoA carboxylase** resistant to **soraphen** A inhibition. are provided as well as methods for purifying fungal **acetyl-CoA carboxylase** resistant to **soraphen** A inhibition. Purified enzyme can be used in assays to identify inhibitors of **soraphen** A resistant **acetyl-CoA carboxylase.**

IT **9075-71-2, Biotin carboxylase**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(selection, cloning and purification of yeast **acetyl-CoA carboxylase** resistant to **soraphen** A)

IT **122547-72-2, Soraphen** A
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(selection, cloning and purification of yeast **acetyl-CoA carboxylase** resistant to **soraphen** A)

FILE 'MEDLINE' ENTERED AT 11:25:07 ON 06 MAR 2006

FILE 'BIOSIS' ENTERED AT 11:25:07 ON 06 MAR 2006

FILE 'EMBASE' ENTERED AT 11:25:07 ON 06 MAR 2006

FILE 'WPIDS' ENTERED AT 11:25:07 ON 06 MAR 2006

FILE 'CONFSCI' ENTERED AT 11:25:07 ON 06 MAR 2006

FILE 'SCISEARCH' ENTERED AT 11:25:07 ON 06 MAR 2006

FILE 'JICST-EPLUS' ENTERED AT 11:25:07 ON 06 MAR 2006

FILE 'JAPIO' ENTERED AT 11:25:07 ON 06 MAR 2006

L9 10 S L8
L10 4 DUP REM L9 (6 DUPLICATES REMOVED)

L10 ANSWER 1 OF 4 EMBASE
ACCESSION NUMBER: 2005382868 EMBASE
TITLE: **Acetyl-coenzyme A carboxylase**: Crucial metabolic enzyme and attractive target for drug discovery.
AUTHOR: Tong L.
CORPORATE SOURCE: L. Tong, Department of Biological Sciences, Columbia University, New York, NY 10027, United States. tong@como.bio.columbia.edu
SOURCE: Cellular and Molecular Life Sciences, (2005) Vol. 62, No. 16, pp. 1784-1803. .
Refs: 127
ISSN: 1420-682X CODEN: CMLSFI
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050922
Last Updated on STN: 20050922

AB **Acetyl-coenzyme A carboxylases** (**ACCs**) have crucial roles in fatty acid metabolism in most living organisms. Mice deficient in ACC2 have continuous fatty acid oxidation and reduced body fat and body weight, validating this enzyme as a target for drug development against obesity, diabetes and other symptoms of the metabolic syndrome. **ACC** is a biotin-dependent enzyme and catalyzes the carboxylation of acetyl-CoA to produce malonyl-CoA through its two catalytic activities, **biotin carboxylase** (**BC**) and carboxyltransferase (CT). **ACC** is a multi-subunit enzyme in most prokaryotes, whereas it is a large, multi-domain enzyme in most eukaryotes. The activity of the enzyme can be controlled at the transcriptional level as well as by small molecule modulators and covalent modification. This review will summarize the structural information that is now available for both the **BC** and CT enzymes, as well as the molecular mechanism of action of potent **ACC** inhibitors. The current intense research on these enzymes could lead to the development of novel therapies against metabolic syndrome and other diseases. .COPYRGT. Birkhauser Verlag, 2005.

L10 ANSWER 2 OF 4 WPIDS
ACCESSION NUMBER: 2004-180421 [17] WPIDS
DOC. NO. NON-CPI: N2004-143468
DOC. NO. CPI: C2004-071370
TITLE: Novel peptide comprising **acetyl CoA carboxylase** (**ACCase**) having deleted biotin binding domain and carboxy transferase domain, and having functional **biotin**

carboxylase domain, useful for identifying **ACCase** inhibitors/activators.

DERWENT CLASS: B04 C07 D16 S03
INVENTOR(S): ELICH, T E; VOLRATH, S L; WEATHERLY, S C; ELICH, T D
PATENT ASSIGNEE(S): (ELIC-I) ELICH T E; (VOLR-I) VOLRATH S L; (WEAT-I) WEATHERLY S C; (CROP-N) CROPSOLUTION INC
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004013159	A2	20040212	(200417)*	EN	56
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2004086994	A1	20040506	(200430)		
AU 2003263980	A1	20040223	(200453)		
EP 1572722	A2	20050914	(200560)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
JP 2006500013	W	20060105	(200603)		34

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004013159	A2	WO 2003-US24356	20030804
US 2004086994	A1 Provisional	US 2002-401170P	20020805
		US 2003-633835	20030804
AU 2003263980	A1	AU 2003-263980	20030804
EP 1572722	A2	EP 2003-767154	20030804
		WO 2003-US24356	20030804
JP 2006500013	W	WO 2003-US24356	20030804
		JP 2004-526405	20030804

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003263980	A1 Based on	WO 2004013159
EP 1572722	A2 Based on	WO 2004013159
JP 2006500013	W Based on	WO 2004013159

PRIORITY APPLN. INFO: US 2002-401170P 20020805; US 2003-633835 20030804

AN 2004-180421 [17] WPIDS

AB WO2004013159 A UPAB: 20040310

NOVELTY - A peptide (I) comprising an **acetyl CoA carboxylase** (**ACCase**) having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional **biotin carboxylase** domain, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising an aqueous carrier solution and (I) solubilized in the aqueous carrier solution, with the peptide included

in the composition in an amount of 0.001 ng-20 mg/ml of aqueous carrier solution, the peptide having a **soraphen** dissociation constant in the composition from 10(-7)-10(-14) M, and the composition having a pH from 5-9;

(2) a nucleic acid (II) to encoding (I);

(3) a recombinant host cell that contains (II) and expresses the encoded peptide;

(4) a kit (III) comprising a first peptide of (I), in combination with a second peptide of (I), where the first and second peptides are from different species; and

(5) a kit comprising a first peptide of (I), in combination with a second peptide comprising an **ACCase** having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a non-functional **biotin-carboxylase** domain, where the first and second peptide are from the same species.

USE - (I) is useful for identifying **Acetyl CoA carboxylase** inhibitors or activators, which involves combining (I) and a compound to be tested for the ability to bind to the **biotin carboxylase** domain, under conditions that permit binding to the **biotin carboxylase** domain, determining whether or not the compound binds to the **biotin carboxylase** domain, the presence of binding indicating the compound is or may be an **Acetyl CoA carboxylase** inhibitor or activator. The method further involves employing the identified binding compound in an assay to detect inhibition or enhancement of **Acetyl CoA carboxylase** activity, and selecting a compound that inhibits or activates **Acetyl CoA carboxylase** activity. (I) is also useful for identifying fungicides, which involves combining (I) and a compound to be tested for the ability to bind to the **biotin carboxylase** domain, under conditions that permit binding to the **biotin carboxylase** domain, determining whether or not the compound binds to the **biotin carboxylase** domain, the presence of binding indicating the compound is or may be fungicide, employing the identified compound in an assay to detect inhibition of **Acetyl CoA carboxylase** activity, and selecting a compound that inhibits **Acetyl CoA carboxylase** activity (claimed).

DESCRIPTION OF DRAWING(S) - The figure shows the binding of (3H)-**soraphen** A and **soraphen** C conjugates to Ustilago **ACCase BC** domain and the full-length Ustilago **ACCase** protein.

Dwg.15/17

L10 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004635728 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15610732

TITLE: A mechanism for the potent inhibition of eukaryotic **acetyl-coenzyme A carboxylase** by **soraphen** A, a macrocyclic polyketide natural product.

AUTHOR: Shen Yang; Volrath Sandra L; Weatherly Stephanie C; Elich Tedd D; Tong Liang

CORPORATE SOURCE: Department of Biological Sciences, Columbia University, New York, NY 10027, USA.

CONTRACT NUMBER: 1R43DK068962-01 (NIDDK)
DK67238 (NIDDK)

SOURCE: Molecular cell, (2004 Dec 22) Vol. 16, No. 6, pp.

Searcher : Shears 571-272-2528

881-91.
Journal code: 9802571. ISSN: 1097-2765.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1W93; PDB-1W96
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20041222
Last Updated on STN: 20050211
Entered Medline: 20050210

AB **Acetyl-coenzyme A carboxylases** (**ACCs**) have crucial roles in fatty acid metabolism. **Soraphen** A, a macrocyclic polyketide natural product, is a nanomolar inhibitor against the **biotin carboxylase** (**BC**) domain of human, yeast, and other eukaryotic **ACCs**. Here we report the crystal structures of the yeast **BC** domain, alone and in complex with **soraphen** A. **Soraphen** has extensive interactions with an allosteric site, about 25 A from the active site. The specificity of **soraphen** is explained by large structural differences between the eukaryotic and prokaryotic **BC** in its binding site, confirmed by our studies on the effects of single-site mutations in this binding site. Unexpectedly, our structures suggest that **soraphen** may bind in the **BC** dimer interface and inhibit the **BC** activity by disrupting the oligomerization of this domain. Observations from native gel electrophoresis confirm this structural insight. The structural information provides a foundation for structure-based design of new inhibitors against these enzymes.

L10 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004234120 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14766011
TITLE: Expression and characterization of recombinant fungal **acetyl-CoA carboxylase** and isolation of a **soraphen**-binding domain.
AUTHOR: Weatherly Stephanie C; Volrath Sandra L; Elich Tedd D
CORPORATE SOURCE: Cropsolution, Inc., P.O. Box 14069, Research Triangle Park, NC 27560, USA.
SOURCE: The Biochemical journal, (2004 May 15) Vol. 380, No. Pt 1, pp. 105-10.
Journal code: 2984726R. E-ISSN: 1470-8728.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AY444507
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 20040511
Last Updated on STN: 20041027
Entered Medline: 20041026

AB **Acetyl-CoA carboxylase** (**ACC**) catalyses the first step in fatty-acid biosynthesis. Owing to its role in primary metabolism, **ACC** has been exploited as a commercial herbicide target and identified as a chemically validated fungicide target. In animals, **ACC** is also a key regulator of fat metabolism. This function has made **ACC** a prime target for the development of anti-obesity and anti-Type II diabetes therapeutics. Despite its economic importance, there is a lack of

published information on recombinant expression of **ACC**. We report here the expression of enzymically active fungal (Ustilago maydis) **ACC** in Escherichia coli. The recombinant enzyme exhibited Km values of 0.14+/-0.013 mM and 0.19+/-0.041 mM for acetyl-CoA and ATP respectively, which are comparable with those reported for the endogenous enzyme. The polyketide natural product **soraphen** is a potent inhibitor of the **BC** (**biotin carboxylase**) domain of endogenous fungal **ACC**. Similarly, recombinant **ACC** activity was inhibited by **soraphen** with a K(i) of 2.1+/-0.9 nM. A truncated **BC** domain that included amino acids 2-560 of the full-length protein was also expressed in E. coli. The isolated **BC** domain was expressed to higher levels, and was more stable than full-length **ACC**. Although incapable of enzymic turnover, the **BC** domain exhibited high-affinity **soraphen** binding (Kd 1.1+/-0.3 nM), demonstrating a native conformation. Additional **BC** domains from the phytopathogenic fungi Magnaporthe grisea and Phytophthora infestans were also cloned and expressed, and were shown to exhibit high-affinity **soraphen** binding. Together, these reagents will be useful for structural studies and assay development.

FILE 'USPATFULL' ENTERED AT 11:26:18 ON 06 MAR 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 2 Mar 2006 (20060302/PD)
FILE LAST UPDATED: 2 Mar 2006 (20060302/ED)
HIGHEST GRANTED PATENT NUMBER: US7007305
HIGHEST APPLICATION PUBLICATION NUMBER: US2006048257
CA INDEXING IS CURRENT THROUGH 28 Feb 2006 (20060228/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 2 Mar 2006 (20060302/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005

L1 17 SEA FILE=REGISTRY ABB=ON PLU=ON ACETYL COA CARBOXYLASE ?/CN
L2 135 SEA FILE=REGISTRY ABB=ON PLU=ON BIOTIN CARBOXYLASE?/CN
L5 19 SEA FILE=REGISTRY ABB=ON PLU=ON "SORAPHEN A"/CN OR ("SORAPHEN A1A"/CN OR "SORAPHEN B"/CN OR "SORAPHEN C"/CN OR "SORAPHEN D"/CN OR "SORAPHEN E"/CN OR "SORAPHEN F"/CN OR "SORAPHEN H"/CN OR "SORAPHEN J"/CN OR "SORAPHEN M"/CN OR "SORAPHEN N"/CN) OR ("SORAPHEN Q"/CN OR "SORAPHEN R"/CN OR "SORAPHEN S"/CN OR "SORAPHEN T"/CN OR "SORAPHEN U"/CN OR "SORAPHEN V"/CN OR "SORAPHEN X"/CN OR "SORAPHEN Y"/CN OR "SORAPHEN Z"/CN)
L6 8201 SEA FILE=CAPLUS ABB=ON PLU=ON L1 OR (AC OR ACETYL)(W)(COA OR (COENZYME OR CO ENZYME OR CO)(W)A)(W)CARBOXYLASE OR ACCASE OR ACC
L11 1550 SEA FILE=USPATFULL ABB=ON PLU=ON L6(L)(L2 OR BIOTIN CARBOXYLASE OR BC)
L12 8 SEA FILE=USPATFULL ABB=ON PLU=ON L11(L)(L5 OR SORAPHEN)

L12 ANSWER 1 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2004:239735 USPATFULL
TITLE: Heterologous production of polyketides
INVENTOR(S): Santi, Daniel, San Francisco, CA, UNITED STATES
Dayem, Linda, San Anselmo, CA, UNITED STATES
Kealey, James, San Anselmo, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004185541	A1	20040923
APPLICATION INFO.:	US 2004-829897	A1	20040421 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-942407, filed on 29 Aug 2001, PENDING Division of Ser. No. US 2000-699136, filed on 27 Oct 2000, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-161703P	19991027 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MORRISON & FOERSTER LLP, 3811 VALLEY CENTRE DRIVE, SUITE 500, SAN DIEGO, CA, 92130-2332
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 3330
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Recombinant host cells that comprise recombinant DNA expression vectors that drive expression of a product and a precursor for biosynthesis of that product can be used to produce useful products such as polyketides in host cells that do not naturally produce the product or produce the product or precursor at low levels due to the absence of the precursor or the presence of the precursor in rate limiting amounts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 2 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2004:209324 USPATFULL
TITLE: Use of acetyl-coa carboxylase for identifying compounds that have an insecticidal effect
INVENTOR(S): Fischer, Reiner, Monheim, GERMANY, FEDERAL REPUBLIC OF
Franken, Eva-Maria, Burlingame, CA, UNITED STATES
Nauen, Ralf, Langenfeld, GERMANY, FEDERAL REPUBLIC OF
Teuschel, Ute, Leverkusen, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004161757	A1	20040819
APPLICATION INFO.:	US 2004-450224	A1	20040224 (10)
	WO 2001-EP14108		20011203

	NUMBER	DATE
PRIORITY INFORMATION:	DE 2000-10062422	20001214

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Bayer CropScience, Patent Department, 100 Bayer Road, Pittsburgh, PA, 15205-9741
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Page(s)
LINE COUNT: 1860

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to nucleic acids which encode insect polypeptides with the biological activity of acetyl-CoA carboxylases, to the polypeptides encoded by them, and to their use for identifying novel, insecticidally active compounds. The invention furthermore relates to methods of finding modulators of these polypeptides, and to the use of these compounds as inhibitors of insect ACCase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 3 OF 8 USPATFULL on STN

ACCESSION NUMBER: 2004:114155 USPATFULL

TITLE: Recombinant biotin carboxylase domains for identification of Acetyle CoA carboxylase inhibitors

INVENTOR(S): Elich, Tedd E., Durham, NC, UNITED STATES
Volrath, Sandra L., Durham, NC, UNITED STATES
Weatherly, Stephanie C., Durham, NC, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004086994	A1	20040506	
APPLICATION INFO.:	US 2003-633835	A1	20030804	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2002-401170P	20020805	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 21 Drawing Page(s)
LINE COUNT: 6645

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A peptide comprising an Acetyl CoA carboxylase (ACCase) having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional biotin carboxylase (BC) domain is described. A nucleic acid that encodes the peptide described above and a recombinant host cell that contains the nucleic acid and expresses the encoded peptide is also described. A method of identifying Acetyl CoA carboxylase inhibitors, fungicides, and herbicides is also described herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 4 OF 8 USPATFULL on STN

ACCESSION NUMBER: 2004:7438 USPATFULL

TITLE: Heterologous production of polyketides

INVENTOR(S): Santi, Daniel V., San Francisco, CA, UNITED STATES
Khosla, Chaitan, Stanfrod, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004005672	A1	20040108	
APPLICATION INFO.:	US 2003-371475	A1	20030221	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-358936P	20020222 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Kosan Biosciences, Inc., Intellectual Property Department, 3832 Bay Center Place, Hayward, CA, 94545
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Page(s)
LINE COUNT: 3491
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Recombinant host cells that comprise recombinant DNA expression vectors that drive expression of a product and a precursor for biosynthesis of that product can be used to produce useful products such as polyketides in host cells that do not naturally produce the product or produce the product or precursor at low levels due to the absence of the precursor or the presence of the precursor in rate limiting amounts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 5 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2003:207984 USPATFULL
TITLE: Treatment of metabolic diseases with soraphen derivatives
INVENTOR(S): Gubler, Marcel, Arlesheim, SWITZERLAND
Mizrahi, Jacques, Basle, SWITZERLAND

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003144345	A1	20030731	
APPLICATION INFO.:	US 2002-197078	A1	20020717	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2001-118316	20010727

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HOFFMANN-LA ROCHE INC., PATENT LAW DEPARTMENT, 340 KINGSLAND STREET, NUTLEY, NJ, 07110
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 761
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the use of Soraphen derivatives and pharmaceutically acceptable esters thereof, for the treatment and/or prophylaxis of diseases which are associated with ACCβ activity and/or fatty acid oxidation such as diabetes, obesity and dyslipidemia.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 6 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2002:258831 USPATFULL
TITLE: Isolated gene for methylmalonyl CoA epimerase and uses thereof
INVENTOR(S): Santi, Daniel, San Francisco, CA, UNITED STATES

Dayem, Linda, Belmont, CA, UNITED STATES
Kealey, James, San Rafael, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002142401	A1	20021003
APPLICATION INFO.:	US 2001-942407	A1	20010829 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-699136, filed on 27 Oct 2000, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-161703P	19991027 (60)
	US 1999-161414P	19991025 (60)
	US 2000-206082P	20000518 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Carolyn A. Favorito, Morrison & Foerster LLP, Suite 500, 3811 Valley Centre Drive, San Diego, CA, 92130-2332
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 3389
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Recombinant host cells that comprise recombinant DNA expression vectors that drive expression of a product and a precursor for biosynthesis of that product can be used to produce useful products such as polyketides in host cells that do not naturally produce the product or produce the product or precursor at low levels due to the absence of the precursor or the presence of the precursor in rate limiting amounts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 7 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2000:160771 USPATFULL
TITLE: Method for identifying inhibitors of soraphen A resistant acetyl-coenzyme a carboxylase
INVENTOR(S): Vahlensieck, Hans-Friedrich, Basel, Switzerland
Hinnen, Albert, Jena, Germany, Federal Republic of
PATENT ASSIGNEE(S): Novartis Finance Corporation, New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6153374		20001128
APPLICATION INFO.:	US 1995-469708		19950606 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-354973, filed on 13 Dec 1994, now patented, Pat. No. US 5641666
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Gitomer, Ralph
LEGAL REPRESENTATIVE: Stults, Larry W.
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 739
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An assay to identify inhibitors of soraphen A resistant

acetyl-coenzyme A carboxylase comprising measuring the reactivity of acetyl-coenzyme A carboxylase in the presence and in the absence of a compound suspected to inhibit soraphen A resistant acetyl-coenzyme A carboxylase reactivity, and comparing the reactivity measurements to identify inhibitors of soraphen A resistant acetyl-coenzyme A carboxylase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 8 OF 8 USPATFULL on STN
ACCESSION NUMBER: 97:54118 USPATFULL
TITLE: Soraphen A resistant fungi and acetyl-CoA carboxylase
INVENTOR(S): Vahlensieck, Hans-Friedrich, Basel, Switzerland
Hinnen, Albert, Jena, Germany, Federal Republic of
PATENT ASSIGNEE(S): Novartis Corporation, Tarrytown, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5641666		19970624	
APPLICATION INFO.:	US 1994-354973		19941213	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1993-25819	19931217

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Wax, Robert A.
ASSISTANT EXAMINER: Lau, Kawai
LEGAL REPRESENTATIVE: Pace, Gary M.
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
LINE COUNT: 867
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention discloses DNA molecules comprising a gene encoding yeast acetyl-coenzyme A carboxylase resistant to soraphen A inhibition. Mutations confering soraphen A resistance to acetyl-CoA carboxylase can be dominant or recessive, and they can be point mutations, deletion or insertion mutations. In addition methods of isolating a gene encoding fungal acetyl-coenzyme A carboxylase resistant to soraphen A inhibition are provided as well as methods for purifying fungal acetyl-coenzyme A carboxylase resistant to soraphen A inhibition. Purified enzyme can be used in assays to identify inhibitors of soraphen A resistant acetyl-coenzyme A carboxylase.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, USPATFULL' ENTERED AT 11:28:05 ON 06 MAR 2006)
L13 107 S "ELICH T"?/AU
L14 146 S "VOLRATH S"?/AU
L15 28 S "WEATHERLY S"?/AU
L16 14 S L13 AND L14 AND L15
L17 14 S L13 AND (L14 OR L15)
L18 14 S L14 AND L15
L19 15 S (L13 OR L14 OR L15) AND L7
L20 15 S L16 OR L17 OR L18 OR L19

- Author(s)

L21 6 DUP REM L20 (9 DUPLICATES REMOVED)

L21 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:149488 CAPLUS
DOCUMENT NUMBER: 144:187043
TITLE: Crystal structure of **biotin carboxylase** domain of **acetyl-coenzyme A carboxylase** and its use for molecular modeling of modulators
INVENTOR(S): Shen, Yang; **Volrath, Sandra L.; Weatherly, Stephanie C.; Elich, Tedd D.**; Anderson, Richard; Tong, Liang
PATENT ASSIGNEE(S): Cropsolution, Inc., USA
SOURCE: PCT Int. Appl., 483 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006017515	A2	20060216	WO 2005-US27440	20050803

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-599831P P 20040806
US 2004-637068P P 20041217

AB The crystal structure atomic coordinates are provided for a **biotin carboxylase** (**BC**) domain of yeast **acetyl-CoA carboxylase** (**ACC**) as free enzyme at 2.9 Å resolution and in complex with soraphen A at 1.8 Å resolution. Homol. modeling of yeast **ACC** may be employed to solve the structures of **BC** domains of other **ACC** species, including those of Magnaporthe, Ustilago maydis, Phytophthora infestans, human ACC1 and ACC2, and mouse. The invention also provides computer-based methods for identifying compds. that modulates activity of **ACC**, a computer-based method for rationally designing a compound that modulates activity of **ACC**, along with compds. produced by such methods. The structures suggest that soraphen may have a novel mechanism of inhibiting the **BC** domain by binding in the dimer interface, thereby disrupting the oligomerization of this domain, which is crucial for its catalytic activity. A fluorescence-based binding assay allowed characterization of the effects of single site mutations in the soraphen binding site on inhibitor sensitivity. Agrochem. and pharmaceutical uses of **ACC** modulators are also provided (no data).

L21 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:120870 CAPLUS
DOCUMENT NUMBER: 140:176293
TITLE: Sequences of fungal and human **acetyl CoA carboxylase** and recombinant **biotin carboxylase** domains for identification of **acetyl CoA carboxylase** inhibitors
INVENTOR(S): **Elich, Tedd D.; Volrath, Sandra L.; Weatherly, Stephanie C.**
PATENT ASSIGNEE(S): Cropsolution, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013159	A2	20040212	WO 2003-US24356	20030804
WO 2004013159	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2494268	AA	20040212	CA 2003-2494268	20030804
US 2004086994	A1	20040506	US 2003-633835	20030804
EP 1572722	A2	20050914	EP 2003-767154	20030804
EP 1572722	A3	20051102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006500013	T2	20060105	JP 2004-526405	20030804
PRIORITY APPLN. INFO.:			US 2002-401170P P	20020805
			WO 2003-US24356 W	20030804

AB A peptide comprising an **Acetyl CoA carboxylase** (**ACCase**) having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional **biotin carboxylase** (**BC**) domain is described. **ACCase** is selected from the group consisting of mammal, insect, yeast, Ascomycota, Basidiomycota, and Oomycota **ACCase**. The protein sequence of the peptide described above and a recombinant host cell that contains the nucleic acid and expresses the encoded peptide is also described. A method of identifying **Acetyl CoA carboxylase** inhibitors, fungicides, is also described herein.

L21 ANSWER 3 OF 6 USPATFULL on STN
ACCESSION NUMBER: 2004:114155 USPATFULL

TITLE: Recombinant **biotin carboxylase** domains for identification of Acetyle CoA carboxylase inhibitors

INVENTOR(S): **Elich, Tedd E.**, Durham, NC, UNITED STATES
Volrath, Sandra L., Durham, NC, UNITED STATES
Weatherly, Stephanie C., Durham, NC, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004086994	A1	20040506
APPLICATION INFO.:	US 2003-633835	A1	20030804 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-401170P	20020805 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 21 Drawing Page(s)
LINE COUNT: 6645

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A peptide comprising an **Acetyl CoA carboxylase** (**ACCase**) having a deleted biotin binding domain, having a deleted carboxy transferase domain, and having a functional **biotin carboxylase** (**BC**) domain is described. A nucleic acid that encodes the peptide described above and a recombinant host cell that contains the nucleic acid and expresses the encoded peptide is also described. A method of identifying **Acetyl CoA carboxylase** inhibitors, fungicides, and herbicides is also described herein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L21 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2005:38098 CAPLUS
DOCUMENT NUMBER: 142:214253

TITLE: A mechanism for the potent inhibition of eukaryotic **acetyl-coenzyme A carboxylase** by soraphen A, a macrocyclic polyketide natural product

AUTHOR(S): Shen, Yang; **Volrath, Sandra L.**; **Weatherly, Stephanie C.**; **Elich, Tedd D.**; Tong, Liang
CORPORATE SOURCE: Department of Biological Sciences, Columbia University, New York, NY, 10027, USA

SOURCE: Molecular Cell (2004), 16(6), 881-891
CODEN: MOCEFL; ISSN: 1097-2765
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Acetyl-CoA carboxylases** (**ACCs**) have crucial roles in fatty acid metabolism Soraphen A, a macrocyclic polyketide natural product, is a nanomolar inhibitor against the

biotin carboxylase (**BC**) domain of human, yeast, and other eukaryotic **ACCs**. Here we report the crystal structures of the yeast **BC** domain, alone and in complex with soraphen A. Soraphen has extensive interactions with an allosteric site, about 25 Å from the active site. The specificity of soraphen is explained by large structural differences between the eukaryotic and prokaryotic **BC** in its binding site, confirmed by our studies on the effects of single-site mutations in this binding site. Unexpectedly, our structures suggest that soraphen may bind in the **BC** dimer interface and inhibit the **BC** activity by disrupting the oligomerization of this domain. Observations from native gel electrophoresis confirm this structural insight. The structural information provides a foundation for structure-based design of new inhibitors against these enzymes.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2004:468907 CAPLUS
DOCUMENT NUMBER: 141:152893
TITLE: Expression and characterization of recombinant fungal **acetyl-CoA carboxylase** and isolation of a soraphen-binding domain
AUTHOR(S): **Weatherly, Stephanie C.; Volrath, Sandra L.; Elich, Tedd D.**
CORPORATE SOURCE: Cropsolution, Inc., Research Triangle Park, NC, 27560, USA
SOURCE: Biochemical Journal (2004), 380(1), 105-110
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Actyl-CoA carboxylase (**ACC**) catalyzes the 1st step in fatty acid biosynthesis. Owing to its role in primary metabolism, **ACC** has been exploited as a com. herbicide target and identified as a chemical validated fungicide target. In animals, **ACC** is also a key regulator of lipid metabolism This function has made **ACC** a prime target for the development of antiobesity and anti-type II diabetes therapeutics. Despite its economic importance, there is a lack of published information on the recombinant expression of **ACC**. Here, the authors report the expression of enzymically active fungal (Ustilago maydis) **ACC** in Escherichia coli. The recombinant enzyme exhibited Km values of 0.14 and 0.19 mM for acetyl-CoA and ATP resp., which were comparable with those reported for the endogenous enzyme. The polyketide natural product, soraphen A, is a potent inhibitor of the **biotin carboxylase** (**BC**) domain of endogenous fungal **ACC**. Similarly, recombinant **ACC** activity was inhibited by soraphen A with a Ki of 2.1 nM. A truncated **BC** domain that included amino acids 2-560 of the full-length protein was also expressed in E. coli. The isolated **BC** domain was expressed to higher levels, and was more stable than full-length **ACC**. Although incapable of enzymic turnover, the **BC** domain exhibited high-affinity soraphen A binding (Kd = 1.1 nM), demonstrating a native conformation. Addnl. **BC** domains from the phytopathogenic fungi, Magnaporthe grisea and Phytophthora infestans, were also cloned and expressed, and were shown to exhibit high-affinity soraphen A binding.

Together, these reagents will be useful for structural studies and assay development.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 6 USPATFULL on STN

ACCESSION NUMBER: 2002:100183 USPATFULL

TITLE: METHODS FOR CONTROLLING GIBBERELLIN LEVELS

INVENTOR(S): BROWN, SHERRI M., CHESTERFIELD, MO, UNITED STATES
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PILLER, KENNETH J., ST LOUIS, MO, UNITED STATES
RAO, SUDABATHULA, ST LOUIS, MO, UNITED STATES
REAM, JOEL E., ST LOUIS, MO, UNITED STATES

PATENT ASSIGNEE(S): ARNOLD WHITE & DURKEE (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002053095	A1	20020502	
	US 6723897	B2	20040420	
APPLICATION INFO.:	US 1999-371307	A1	19990810	(9)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Melinda Patterson, HOWREY SIMON ARNOLD & WHITE, LLP, 750 Bering Drive, Houston, TX, 77057

NUMBER OF CLAIMS: 79

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 43 Drawing Page(s)

LINE COUNT: 8723

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and materials are disclosed for the inhibition and control of gibberellic acid levels. In particular, nucleic acid sequences of copalyl diphosphate synthase, 3-β hydroxylase, and 2-oxidase and additional nucleic acid sequences are disclosed. Gibberellic acid levels may be inhibited or controlled by preparation of a chimeric expression construct capable of expressing a RNA or protein product which suppresses the gibberellin biosynthetic pathway sequence, diverts substrates from the pathway or degrades pathway substrates or products. The sequence is preferably a copalyl diphosphate synthase sequence, a 3β-hydroxylase sequence, a 2-oxidase sequence, a phytoene synthase sequence, a C20-oxidase sequence, and a 2β,3β-hydroxylase sequence. Administration of a complementing agent, preferably a gibberellin or gibberellin precursor or intermediate restores bioactivity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

FILE 'HOME' ENTERED AT 11:31:24 ON 06 MAR 2006

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=> d his ful

     (FILE 'CAPLUS' ENTERED AT 10:49:28 ON 06 MAR 2006)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 11:11:42 ON 06 MAR 2006
               E ACETYL COA CARBOXYLASE/CN 5
L1           17 SEA ABB=ON  PLU=ON  ACETYL COA CARBOXYLASE ?/CN
               E BIOTIN CARBOXYLASE/CN 5
L2          135 SEA ABB=ON  PLU=ON  BIOTIN CARBOXYLASE?/CN
               E SORAPHEN/CN
L3            1 SEA ABB=ON  PLU=ON  "SORAPHEN A"/CN
               E SORAPHENS/CN 5
L4            1 SEA ABB=ON  PLU=ON  128481-23-2/RN
               D CN
               E SORAPHEN/CN
L5           19 SEA ABB=ON  PLU=ON  "SORAPHEN A"/CN OR ("SORAPHEN A1A
               "/CN OR "SORAPHEN B"/CN OR "SORAPHEN C"/CN OR "SORAPHEN
               D"/CN OR "SORAPHEN E"/CN OR "SORAPHEN F"/CN OR "SORAPHEN
               H"/CN OR "SORAPHEN J"/CN OR "SORAPHEN M"/CN OR "SORAPHEN
               N"/CN) OR ("SORAPHEN Q"/CN OR "SORAPHEN R"/CN OR "SORAPHEN
               S"/CN OR "SORAPHEN T"/CN OR "SORAPHEN U"/CN OR "SORAPHEN
               V"/CN OR "SORAPHEN X"/CN OR "SORAPHEN Y"/CN OR "SORAPHEN
               Z"/CN)

     FILE 'CAPLUS' ENTERED AT 11:18:28 ON 06 MAR 2006
L6         8201 SEA ABB=ON  PLU=ON  L1 OR (AC OR ACETYL)(W)(COA OR
               (COENZYME OR CO ENZYME OR CO)(W)A)(W)CARBOXYLASE OR ACCASE
               OR ACC
L7          145 SEA ABB=ON  PLU=ON  L6 AND (L2 OR BIOTIN CARBOXYLASE OR
               BC)
L8            5 SEA ABB=ON  PLU=ON  L7 AND (L5 OR SORAPHEN)
L*** DEL      4 S L8 AND ELICH ?/AU

     FILE 'REGISTRY' ENTERED AT 11:24:05 ON 06 MAR 2006

     FILE 'CAPLUS' ENTERED AT 11:24:05 ON 06 MAR 2006
               D QUE L8
               D 1-5 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 11:25:07 ON 06 MAR 2006
L9           10 SEA ABB=ON  PLU=ON  L8
L10           4 DUP REM L9 (6 DUPLICATES REMOVED)
               D 1-4 IBIB ABS

     FILE 'USPATFULL' ENTERED AT 11:26:18 ON 06 MAR 2006
L11        1550 SEA ABB=ON  PLU=ON  L6(L)(L2 OR BIOTIN CARBOXYLASE OR BC)
L12           8 SEA ABB=ON  PLU=ON  L11(L)(L5 OR SORAPHEN)
               D QUE L12
               D L12 1-8 IBIB ABS

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO, USPATFULL' ENTERED AT 11:28:05 ON 06 MAR 2006
L13          107 SEA ABB=ON  PLU=ON  "ELICH T"?/AU
L14          146 SEA ABB=ON  PLU=ON  "VOLRATH S"?/AU
L15           28 SEA ABB=ON  PLU=ON  "WEATHERLY S"?/AU
L16           14 SEA ABB=ON  PLU=ON  L13 AND L14 AND L15
L17           14 SEA ABB=ON  PLU=ON  L13 AND (L14 OR L15)
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L18          14 SEA ABB=ON  PLU=ON  L14 AND L15
L19          15 SEA ABB=ON  PLU=ON  (L13 OR L14 OR L15) AND L7
L20          15 SEA ABB=ON  PLU=ON  L16 OR L17 OR L18 OR L19
L21           6 DUP REM L20 (9 DUPLICATES REMOVED)
                D 1-6 IBIB ABS

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FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:    5 MAR 2006  HIGHEST RN 875875-45-9
DICTIONARY FILE UPDATES:   5 MAR 2006  HIGHEST RN 875875-45-9

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*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMI
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REGISTRY includes numerically searchable data for experimental and
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FILE CAPLUS

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FILE LAST UPDATED: 5 Mar 2006  (20060305/ED)

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http://www.cas.org/infopolicy.html

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FILE LAST UPDATED: 4 MAR 2006 (20060304/UP). FILE COVERS 1950 TO DAT

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 1 March 2006 (20060301/ED)

FILE EMBASE
FILE COVERS 1974 TO 3 Mar 2006 (20060303/ED)

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FILE WPIDS
FILE LAST UPDATED: 2 MAR 2006 <20060302/UP>
MOST RECENT DERWENT UPDATE: 200615 <200615/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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Searcher : Shears 571-272-2528

DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
FIRST VIEW - FILE WPIFV.
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>>> THE CPI AND EPI MANUAL CODES WILL BE REVISED FROM UPDATE 200601.
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http://www.stn-international.de/stndatabases/details/ipc_reform.html
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

FILE CONFSCI
FILE COVERS 1973 TO 25 May 2005 (20050525/ED)

CSA has suspended updates until further notice,

FILE SCISEARCH

FILE COVERS 1974 TO 2 Mar 2006 (20060302/ED)

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FILE JICST-EPLUS
FILE COVERS 1985 TO 27 FEB 2006 (20060227/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE COVERS APR 1973 TO OCTOBER 27, 2005

>>> GRAPHIC IMAGES AVAILABLE <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOT YET AVAILABLE IN THIS FILE.
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ABOUT THE IPC REFORM <<<

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 2 Mar 2006 (20060302/PD)
FILE LAST UPDATED: 2 Mar 2006 (20060302/ED)
HIGHEST GRANTED PATENT NUMBER: US7007305
HIGHEST APPLICATION PUBLICATION NUMBER: US2006048257
CA INDEXING IS CURRENT THROUGH 28 Feb 2006 (20060228/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 2 Mar 2006 (20060302/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2005

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